```
* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  NOV 21  CAS patent coverage to include exemplified prophetic
                  substances identified in English-, French-, German-,
                  and Japanese-language basic patents from 2004-present
 NEWS  3  NOV 26  MARPAT enhanced with FSORT command
 NEWS  4  NOV 26  CHEMSAFE now available on STN Easy
 NEWS  5  NOV 26  Two new SET commands increase convenience of STN
                  searching
 NEWS  6  DEC 01  ChemPort single article sales feature unavailable
 NEWS  7  DEC 12  GBFULL now offers single source for full-text
                  coverage of complete UK patent families
 NEWS  8  DEC 17  Fifty-one pharmaceutical ingredients added to PS
 NEWS  9  JAN 06  The retention policy for unread STNmail messages
                  will change in 2009 for STN-Columbus and STN-Tokyo
 NEWS 10  JAN 07  WPIDS, WPINDEX, and WPIX enhanced Japanese Patent
                  Classification Data

 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
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* * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 17:15:37 ON 21 JAN 2009

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.22       0.22

FILE 'REGISTRY' ENTERED AT 17:15:52 ON 21 JAN 2009
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STRUCTURE FILE UPDATES:   20 JAN 2009  HIGHEST RN 1094597-78-0
DICTIONARY FILE UPDATES:  20 JAN 2009  HIGHEST RN 1094597-78-0

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TSCA INFORMATION NOW CURRENT THROUGH July 5, 2008.

  Please note that search-term pricing does apply when
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REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
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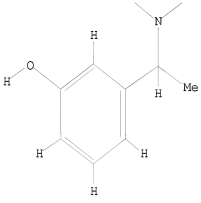
L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1               STR




Structure attributes must be viewed using STN Express query preparation.

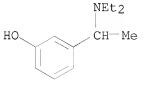
=> s l1 full
FULL SEARCH INITIATED 17:16:11 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    10280 TO ITERATE

100.0% PROCESSED    10280 ITERATIONS                                16 ANSWERS
SEARCH TIME: 00.00.01

L2           16 SEA SSS FUL L1

=> d l2 scan

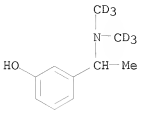
L2   16 ANSWERS   REGISTRY  COPYRIGHT 2009 ACS on STN
IN   Phenol, 3-[1-(diethylamino)ethyl]-
MF   C12 H19 N O




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

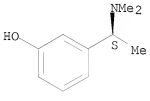
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):10

L2 16 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN Phenol, 3-[1-[di(methyl-d3)amino]ethyl]- (9CI)
MF C10 H9 D6 N O




L2 16 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN Phenol, 3-[(1S)-1-(dimethylamino)ethyl]-, sodium salt (1:1)
MF C10 H15 N O . Na

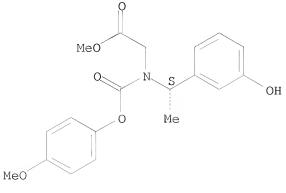
Absolute stereochemistry. Rotation (-).





L2 16 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN Glycine, N-[(1S)-1-(3-hydroxyphenyl)ethyl]-N-[(4-methoxyphenoxy)carbonyl]-, methyl ester
MF C19 H21 N O6

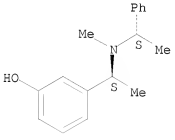
Absolute stereochemistry.



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

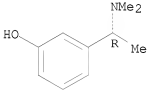
L2 16 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN Phenol, 3-[(1S)-1-[methyl[(1S)-1-phenylethyl]amino]ethyl]-
MF C17 H21 N O

Absolute stereochemistry. Rotation (-).



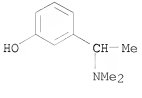

L2 16 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN Phenol, 3-[(1R)-1-(dimethylamino)ethyl]-
MF C10 H15 N O

Absolute stereochemistry.




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

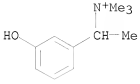
L2 16 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN Phenol, 3-[1-(dimethylamino)ethyl]-, hydrochloride (1:1)
MF C10 H15 N O . Cl H




● HCl

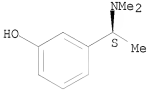
L2 16 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN  Benzenemethanaminium, 3-hydroxy-N,N,N,α-tetramethyl-
MF  C11 H18 N O
CI  COM




L2  16 ANSWERS  REGISTRY  COPYRIGHT 2009 ACS on STN
IN  Phenol, 3-[(1S)-1-(dimethylamino)ethyl]-
MF  C10 H15 N O
CI  COM

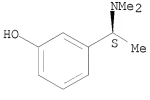
Absolute stereochemistry.  Rotation (-).




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L2  16 ANSWERS  REGISTRY  COPYRIGHT 2009 ACS on STN
IN  Phenol, 3-[(1S)-1-(dimethylamino)ethyl]-, hydrochloride (1:1)
MF  C10 H15 N O . Cl H

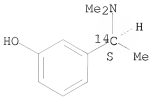
Absolute stereochemistry.  Rotation (-).





L2  16 ANSWERS  REGISTRY  COPYRIGHT 2009 ACS on STN
IN  Phenol, 3-[1-(dimethylamino)ethyl-1-14C]-, (S)- (9CI)
MF  C10 H15 N O

Absolute stereochemistry.




HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

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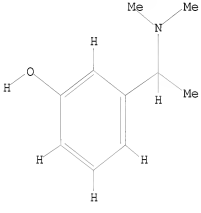
L3 STRUCTURE UPLOADED

=> d l3
L3 HAS NO ANSWERS
L3 STR




Structure attributes must be viewed using STN Express query preparation.

=> s l3 full
FULL SEARCH INITIATED 17:17:43 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 10293 TO ITERATE

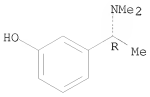
100.0% PROCESSED 10293 ITERATIONS 11 ANSWERS
SEARCH TIME: 00.00.01

L4 11 SEA SSS FUL L3

=> d l4 scan

L4 11 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN Phenol, 3-[(1R)-1-(dimethylamino)ethyl]-
MF C10 H15 N O

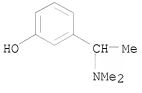
Absolute stereochemistry.




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

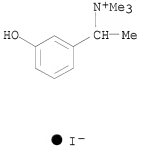
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):10

L4 11 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN Phenol, 3-[1-(dimethylamino)ethyl]-
MF C10 H15 N O
CI COM



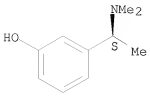

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L4 11 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN Benzenemethanaminium, 3-hydroxy-N,N,N,α-tetramethyl-, iodide (1:1)
MF C11 H18 N O . I



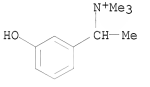

L4 11 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN Phenol, 3-[(1S)-1-(dimethylamino)ethyl]-
MF C10 H15 N O
CI COM

Absolute stereochemistry. Rotation (-).

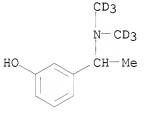



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L4  11 ANSWERS  REGISTRY  COPYRIGHT 2009 ACS on STN
IN  Benzenemethanaminium, 3-hydroxy-N,N,N,α-tetramethyl-
MF  C11 H18 N O
CI  COM

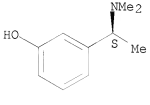



L4  11 ANSWERS  REGISTRY  COPYRIGHT 2009 ACS on STN
IN  Phenol, 3-[1-[di(methyl-d3)amino]ethyl]- (9CI)
MF  C10 H9 D6 N O




L4  11 ANSWERS  REGISTRY  COPYRIGHT 2009 ACS on STN
IN  Phenol, 3-[(1S)-1-(dimethylamino)ethyl]-, hydrochloride (1:1)
MF  C10 H15 N O . Cl H

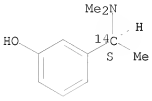
Absolute stereochemistry.  Rotation (-).




● HCl

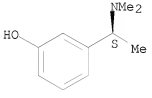
L4  11 ANSWERS  REGISTRY  COPYRIGHT 2009 ACS on STN
IN  Phenol, 3-[1-(dimethylamino)ethyl-1-14C]-, (S)- (9CI)
MF  C10 H15 N O

Absolute stereochemistry.




L4  11 ANSWERS  REGISTRY  COPYRIGHT 2009 ACS on STN
IN  Phenol, 3-[(1S)-1-(dimethylamino)ethyl]-, sodium salt (1:1)
MF  C10 H15 N O . Na

Absolute stereochemistry.  Rotation (-).

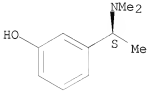




L4  11 ANSWERS  REGISTRY  COPYRIGHT 2009 ACS on STN
IN  Bicyclo[2.2.1]heptane-1-methanesulfonic acid, 7,7-dimethyl-2-oxo-,
    (1S,4R)-, compd. with 3-[(1S)-1-(dimethylamino)ethyl]phenol (1:1)
MF  C10 H16 O4 S . C10 H15 N O

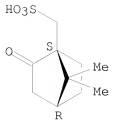
    CM  1

Absolute stereochemistry.  Rotation (-).

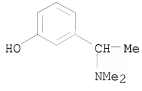



    CM  2

Absolute stereochemistry.  Rotation (+).




L4 11 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN Phenol, 3-[1-(dimethylamino)ethyl]-, hydrochloride (1:1)
MF C10 H15 N O . Cl H




● HCl

ALL ANSWERS HAVE BEEN SCANNED

=> file caplus

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 372.72 | 372.94 |

FILE 'CAPLUS' ENTERED AT 17:18:32 ON 21 JAN 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


FILE COVERS 1907 - 21 Jan 2009 VOL 150 ISS 4
FILE LAST UPDATED: 20 Jan 2009 (20090120/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/legal/infopolicy.html

```
=> s l4
L5          59 L4

=> s l4 and resolution
            59 L4
        108684 RESOLUTION
L6           7 L4 AND RESOLUTION

=> s l4 and optical?
            59 L4
       1146193 OPTICAL?
L7           5 L4 AND OPTICAL?

=> s l7 or l6
L8          11 L7 OR L6

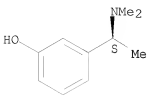
=> d l8 ibib abs hitstr 1-
YOU HAVE REQUESTED DATA FROM 11 ANSWERS - CONTINUE? Y/(N):y

L8   ANSWER 1 OF 11  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2008:1250055  CAPLUS
DOCUMENT NUMBER:          149:471196
TITLE:                    A process for the preparation of rivastigmine or a
                          salt thereof
INVENTOR(S):              Mandava, Venkata Naga Brahmeswara Rao; Vajrala,
                          Venkata Reddy; Varanasi, Ganesh; Adla, Vijay Kumar;
                          Jambula, Mukund Reddy; Kanumathi Reddy, Vijaypal Reddy
PATENT ASSIGNEE(S):       Dr. Reddy's Laboratories Ltd., India; Dr. Reddys
                          Laboratories Inc.
SOURCE:                   Eur. Pat. Appl., 16pp.
                          CODEN: EPXXDW
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
     --------------      ----   --------    --------------------     --------
     EP 1980552           A2    20081015    EP 2008-7105             20080410
     EP 1980552           A3    20081029
          R:  AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,
              IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI,
              SK, TR, AL, BA, MK, RS
     IN 2007CH00758       A     20081128    IN 2007-CH758            20070410
     US 20080255383       A1    20081016    US 2008-100591           20080410
PRIORITY APPLN. INFO.:                       IN 2007-CH758       A    20070410
                                             US 2008-30814       A    20080222
                                             US 2008-30814P      P    20080222
OTHER SOURCE(S):          CASREACT 149:471196
AB   The process comprises reacting S-(-)-[1-(3-
     hydroxyphenyl)ethyl]dimethylamine (I) with N-ethyl-N-methylcarbamoyl
     chloride (II) in the presence of an organic base to obtain a free base of
     rivastigmine.  Rivastigmine tartrate is a known drug.  Thus, reaction of I
     with II in Me iso-Bu ketone in the presence of pyridine and
     tetrabutylammonium bromide gave, after workup, rivastigmine (free base).
IT   139306-10-8P
     RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic
     preparation); PREP (Preparation); RACT (Reactant or reagent)
        (process for preparation of rivastigmine or salt thereof)
RN   139306-10-8  CAPLUS
```

CN Phenol, 3-[(1S)-1-(dimethylamino)ethyl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:396551 CAPLUS
DOCUMENT NUMBER: 148:387367
TITLE: Improved process for the industrial preparation of Rivastigmine hydrogen tartrate and its pharmaceutical polymorphs
INVENTOR(S): Nadkarni, Sunil Sadanand
PATENT ASSIGNEE(S): Torrent Pharmaceuticals Ltd., India
SOURCE: Indian Pat. Appl., 50pp.
CODEN: INXXBQ
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

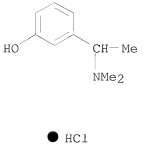
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| IN 2005MU00036 | A | 20060811 | IN 2005-MU36 | 20050114 |
| PRIORITY APPLN. INFO.: | | | IN 2005-MU36 | 20050114 |

OTHER SOURCE(S): CASREACT 148:387367

AB A process for the preparation of rivastigmine hydrogen tartarate starting from α-3-hydroxyphenylethyldimethylamine is described. The present invention is simple, efficient, environmentally safe and a cost effective methodol. for the production of rivastigmine and its pharmaceutical polymorphs. Further, this invention also relates to the solid-state phys. properties of rivastigmine hydrogen tartarate. These properties can be influenced by controlling the conditions under which rivastigmine hydrogen tartarate is obtained in solid form. One example of solid-state phys. properties is the flowability of the milled solid. Flowability affects the ease with which the material is handled during processing into a pharmaceutical product.

IT 5441-61-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(improved process for the industrial preparation of rivastigmine hydrogen tartrate and its pharmaceutical polymorphs)

RN 5441-61-2 CAPLUS
CN Phenol, 3-[1-(dimethylamino)ethyl]-, hydrochloride (1:1) (CA INDEX NAME)

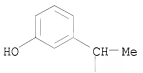


● HCl

L8 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:313129 CAPLUS
DOCUMENT NUMBER: 148:191703
TITLE: Synthesis of S-(+)-rivastigmine hydrogen tartrate
AUTHOR(S): Feng, Jin; Chen, Wei-min; Sun, Ping-hua
CORPORATE SOURCE: Dep. Med. Chem., Sch. Pharmacy, Jinan Univ., Guangzhou, 510632, Peop. Rep. China
SOURCE: Nanfang Yike Daxue Xuebao (2007), 27(2), 177-180
CODEN: NYDXAN; ISSN: 1673-4254
PUBLISHER: Nanfang Yike Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 148:191703

AB The synthesis of the title compound, S-(+)-rivastigmine hydrogen tartrate [i.e., N-ethyl-N-(methyl)carbamic acid 3-[(1S)-1-(dimethylamino)ethyl]phenyl ester, (2R,3R)-2,3-dihydroxybutanedioate] which was known as an agent for the treatment of Alzheimer disease, is reported. S-(+)-rivastigmine hydrogen tartrate was synthesized by using 1-(3-hydroxyphenyl)ethanone as the starting material via oximation, reduction and N-methylation to produce a key intermediate 3-[1-(dimethylamino)ethyl]phenol, which was treated with N-ethyl-N-(methyl)carbamoyl chloride. The enantiomers were resolved with di(+)-p-toluoyl-D-tartaric acid, and the title compound was prepared by mixing S-rivastigmine base with L-(+)-tartrate. The total yield of S-(+)-rivastigmine hydrogen tartrate was 4.17%. The materials in this procedure are all com. available. The reaction conditions are mild and total yield is high.

IT 105601-04-5P, 3-[1-(Dimethylamino)ethyl]phenol
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of chiral rivastigmine hydrogen tartrate via synthetic sequence involving oximation, reduction, methylation, carbamoylation and resolution)
RN 105601-04-5 CAPLUS
CN Phenol, 3-[1-(dimethylamino)ethyl]- (CA INDEX NAME)




L8 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:257897 CAPLUS
DOCUMENT NUMBER: 146:295621
TITLE: Process for preparation of rivastigmine and tartrate
INVENTOR(S): Ma, Dawei; Pan, Qiangbiao; Pan, Song
PATENT ASSIGNEE(S): Shanghai Aobo Bio-Pharmaceutical Technology Co., Ltd, Peop. Rep. China; Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences; Zhejiang Huahai Pharmaceutical Co., Ltd.
SOURCE: PCT Int. Appl., 27pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

| | | | | | |
|---|---|---|---|---|---|
| WO 2007025481 | A1 | 20070308 | WO 2006-CN2246 | | 20060901 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | | |
| CN 1923801 | A | 20070307 | CN 2005-10029393 | | 20050902 |
| CN 100391938 | C | 20080604 | | | |

PRIORITY APPLN. INFO.: CN 2005-10029393 A 20050902

OTHER SOURCE(S): CASREACT 146:295621; MARPAT 146:295621

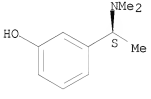
AB The present invention relates to a process for preparing N-ethyl-N-methyl-3-[(1S)-1-(dimethylamino)ethyl]phenyl carbamate (rivastigmine) and its tartrate, which comprises reacting 3-[(1S)-1-(dimethylamino)ethyl]phenol or salts with phosgene, diphosgene or triphosgene, followed by the addition of N-methylethanamine to give rivastigmine. The tartrate was obtained by reacting rivastigmine with L-(+)-tartaric acid. The process has the advantages of high yield and optical purity.

IT 894079-56-2 928216-23-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of rivastigmine and tartrate)

RN 894079-56-2 CAPLUS

CN Phenol, 3-[(1S)-1-(dimethylamino)ethyl]-, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

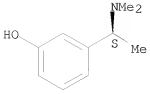



● HCl

RN 928216-23-3 CAPLUS

CN Phenol, 3-[(1S)-1-(dimethylamino)ethyl]-, sodium salt (1:1) (CA INDEX NAME)

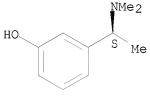
Absolute stereochemistry. Rotation (-).




● Na

IT 139306-10-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of rivastigmine and tartrate)
RN 139306-10-8 CAPLUS
CN Phenol, 3-[(1S)-1-(dimethylamino)ethyl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:436761 CAPLUS
DOCUMENT NUMBER: 144:450512
TITLE: Carbamoylation method for preparation of rivastigmine [(S)-3-[(1-dimethylamino)ethyl]phenyl N-ethyl-N-methylcarbamate]
INVENTOR(S): Gharpure, Milind Moreshwar; Bhawal, Baburao Manikrao; Shah, Viral Bipinbhai; Zope, Umesh Rewaji; Mehta, Satish Ramanlal
PATENT ASSIGNEE(S): Emcure Pharmaceuticals Limited, India
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006048720 | A1 | 20060511 | WO 2005-IB3237 | 20051029 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, | | | | |

CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM

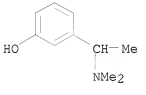
| | | | | | |
|---|---|---|---|---|---|
| IN 2004MU01207 | A | 20071214 | IN 2004-MU1207 | | 20041108 |
| EP 1856036 | A1 | 20071121 | EP 2005-797945 | | 20051029 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | | | |
| BR 2005015767 | A | 20080304 | BR 2005-15767 | | 20051029 |
| JP 2008519023 | T | 20080605 | JP 2007-539647 | | 20051029 |
| KR 2007083814 | A | 20070824 | KR 2007-709495 | | 20070426 |
| PRIORITY APPLN. INFO.: | | | IN 2004-MU1207 | A | 20041108 |
| | | | WO 2005-IB3237 | W | 20051029 |

OTHER SOURCE(S): CASREACT 144:450512

AB Rivastigmine is prepared in high yield and selectivity by the carbamoylation of (S)-3-[1-(dimethylamino)ethyl]phenol with N-ethyl-N-methylcarbamoyl chloride.

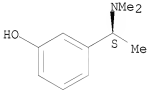
IT 105601-04-5 139306-10-8,
(S)-3-[1-(Dimethylamino)ethyl]phenol
RL: RCT (Reactant); RACT (Reactant or reagent)
(in a carbamoylation method for preparation of rivastigmine [(S)-3-[(1-dimethylamino)ethyl]phenyl N-ethyl-N-methylcarbamate])

RN 105601-04-5 CAPLUS
CN Phenol, 3-[1-(dimethylamino)ethyl]- (CA INDEX NAME)




RN 139306-10-8 CAPLUS
CN Phenol, 3-[(1S)-1-(dimethylamino)ethyl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 2003:972013 CAPLUS |
| DOCUMENT NUMBER: | 140:27668 |
| TITLE: | A process for the preparation of phenyl carbamates |
| INVENTOR(S): | Thennati, Rajamannar |
| PATENT ASSIGNEE(S): | Sun Pharmaceutical Industries Limited, India; Patel, Hetalkumar Virendrabhai |
| SOURCE: | PCT Int. Appl., 20 pp.<br>CODEN: PIXXD2 |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | English |
| FAMILY ACC. NUM. COUNT: | 1 |
| PATENT INFORMATION: | |

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003101917 | A2 | 20031211 | WO 2003-IN210 | 20030602 |
| WO 2003101917 | A3 | 20040812 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| IN 2002MU00484 | A | 20040228 | IN 2002-MU484 | 20020531 |
| IN 2003MU00166 | A | 20050204 | IN 2003-MU166 | 20030206 |
| AU 2003263574 | A1 | 20031219 | AU 2003-263574 | 20030602 |
| US 20060293518 | A1 | 20061228 | US 2006-516104 | 20060807 |
| US 7385076 | B2 | 20080610 | | |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| IN 2002-MU484 | A | 20020531 |
| IN 2003-MU166 | A | 20030206 |
| WO 2003-IN210 | W | 20030602 |

OTHER SOURCE(S): CASREACT 140:27668; MARPAT 140:27668

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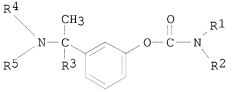


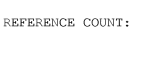
I

AB Phenylcarbamates [I; R1 = H, (un)branched lower (cyclo)alkyl, cyclohexyl, allyl, propargyl, benzyl; R2 = H, Me, Et, propyl; NR1R2 = three-to-eight-membered ring with or without a hetero atom like nitrogen or oxygen; R3 =H, lower alkyl; R4, R5 = lower alkyl; e.g., racemic rivastigmine] are prepared in high yield and selectivity by the reaction of the corresponding I phenol [e.g., 3-[(1-dimethylamino)ethyl]phenol] with a 4-nitrophenylcarbamate 4-O2NC6H4O2CN(R1)R2 (e.g., 4-nitrophenyl N-ethyl-N-methylcarbamate) in the presence of a base (e.g., potassium carbonate).

IT 105601-04-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in a process for the preparation of Ph carbamates)

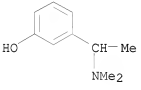
RN 105601-04-5 CAPLUS

CN Phenol, 3-[1-(dimethylamino)ethyl]- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

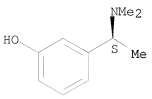
L8 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:429602 CAPLUS
DOCUMENT NUMBER: 136:183572
TITLE: Synthesis of Rivastigmine, a chiral drug for Alzheimer's Disease
AUTHOR(S): Jiang, Yong-wen; Hua, Zheng-mao; Xie, Li-hua; Yang, Li-ping
CORPORATE SOURCE: Department of Chemistry, East China Normal University, Shanghai, 200062, Peop. Rep. China
SOURCE: Huadong Shifan Daxue Xuebao, Ziran Kexueban (2001), (1), 61-65
CODEN: HSZKEO; ISSN: 1000-5641
PUBLISHER: Huadong Shifan Daxue Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 136:183572
AB Rivastigmine, a sort of acetylcholinesterase inhibitor, used in the symptomatic treatment of mild to moderate Alzheimer's Disease, was synthesized from m-hydroxyphenyl Me ketone via three steps, giving racemic product, further chemical resolution with D-tartaric acid derivative, giving the S-product..
IT 105601-04-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of Rivastigmine, a chiral drug for Alzheimer's Disease)
RN 105601-04-5 CAPLUS
CN Phenol, 3-[1-(dimethylamino)ethyl]- (CA INDEX NAME)




L8 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1992:128255 CAPLUS
DOCUMENT NUMBER: 116:128255
ORIGINAL REFERENCE NO.: 116:21695a,21698a
TITLE: A general enantioselective synthesis of α-arylethylamines
AUTHOR(S): Chen, Chung Pin; Prasad, Kapa; Repic, Oljan
CORPORATE SOURCE: Sandoz Res. Inst., East Hanover, NJ, 07936, USA
SOURCE: Tetrahedron Letters (1991), 32(49), 7175-8
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 116:128255
AB Optically active α-arylethylamines were prepared starting from acetophenones in ≥95% ee and ≥70% overall yield using oxazaborolidine catalyzed enantioselective reduction followed by the displacement of the hydroxy group by an azide group with clean inversion under Mitsunobu reaction conditions.
IT 139306-10-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 139306-10-8 CAPLUS

CN Phenol, 3-[(1S)-1-(dimethylamino)ethyl]- (CA INDEX NAME)

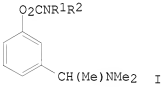
Absolute stereochemistry. Rotation (-).




L8 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 1987:188457 CAPLUS |
| DOCUMENT NUMBER: | 106:188457 |
| ORIGINAL REFERENCE NO.: | 106:30389a,30392a |
| TITLE: | Pharmacological activity of novel anticholinesterase agents of potential use in the treatment of Alzheimer's disease |
| AUTHOR(S): | Weinstock, Marta; Razin, Michal; Chorev, Michael; Tashma, Zeev |
| CORPORATE SOURCE: | Sch. Pharm., Hebrew Univ., Jerusalem, Israel |
| SOURCE: | Advances in Behavioral Biology (1986), 29(Alzheimer's Parkinson's Dis.), 539-49<br>CODEN: ADBBBW; ISSN: 0099-6246 |
| DOCUMENT TYPE: | Journal |
| LANGUAGE: | English |

GI



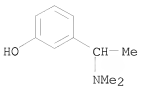
I

AB Eight miotine derivs. I (R1 = H, Me or Et, R2 = alkyl) were prepared by reacting α-m-hydroxyphenylethyldimethylamine [ 105601-04-5 ] with alkyl isocyanates or dialkylaminocarbamyl chlorides. Their ability to inhibit brain acetylcholinesterase (AChE) [9000-81-1] varied 3000-fold and was not related to either the hydrophobicity, molar refractivity, or length of the most extended conformation of the carbamate moiety. Furthermore, no clear correlation could be demonstrated between the anticholinesterase activity in vitro and that obtained ex vivo after injection of the drug into mice. All the novel compds. were relatively more active in vivo in relation to physostigmine or miotine than they were in vitro. Comparison of the acute toxicity of I with that of physostigmine and miotine showed the former to have a higher therapeutic ratio. The I derivs. tested had different anticholinesterase activities in different brain areas; the cerebral cortex enzyme was the most sensitive and the medulla oblongata enzyme was the least sensitive. The use of these compds. for treatment of chronic conditions such as Alzheimer's disease is discussed.

IT 105601-04-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with alkyl isocyanates and dialkylaminocarbamyl chlorides)

RN 105601-04-5 CAPLUS

CN Phenol, 3-[1-(dimethylamino)ethyl]- (CA INDEX NAME)

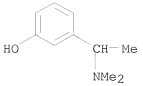



L8 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1933:563 CAPLUS
DOCUMENT NUMBER: 27:563
ORIGINAL REFERENCE NO.: 27:67g-i
TITLE: Resolution of α-m-hydroxyphenylethylmethylamine and the preparation of d- and l-miotine (methylurethans of d- and l-α-m-hydroxyphenylethyldimethylamine)
AUTHOR(S): Macdonald, Joseph McL.; Stedman, Edgar
SOURCE: Journal of the Chemical Society (1932) 2513-19
CODEN: JCSOA9; ISSN: 0368-1769
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

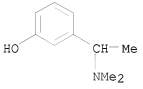
AB cf. Stedman and Stedman, C. A. 23, 3451. In a reinvestigation of the resolution of miotine (I), it was found that in no case could a crystalline salt be prepared m-MeOC6H4CHMeNMe2 also could not be resolved. Attention was then directed to m-HOC6H4CHMeNHMe. m-MeOC6H4CHMeBr and MeNH2 in MeCN give 75% of α-m-methoxyphenylethylmethylamine, b15 117-8°, whose HCl salt m. 152-3°; in EtOH the yield is 63%; the chloride in EtOH gives 54% of the base. HBr gives dl-α-m-hydroxyphenylethylmethylamine (II), m. 160°; HCl salt, m. 160°. While crystalline H d-tartrate and H l-malate salts could be prepared, they were not suitable for resolution. d-Bromocamphor-π-sulfonic acid (III) gave satisfactory results; the III salt of d-II, m. about 193°, crystallizing with 1.5 mols. H2O, resulted from the HCl salt of II and the NH4 salt of III in 79% yield and could be crystallized from H2O; the anhydrous salt from AcOEt m. 197°; the residue from the mother liquor was converted into the HCl salt and treated with l-III, giving the l-III salt of l-II. d-II, m. 171°, [α]D 68° (C5H5N, c 5); HCl salt, m. 201°, [α]D 20° (H2O, c 10); the l-II possessed similar properties. d-II in MeOH and formalin, treated with H2 (PtO2 catalyst), gave d-α-m-hydroxyphenylethyldimethylamine, m. 116°, [α]D 55.8° (EtOH, c 5); HCl salt, m. 161°, [α]D 15.2° (H2O, c 10); the l-isomer was similar. These bases with MeNCO give d- and l-I, m. 85°, [α]D ± 37° (EtOH, c 10); the HCl salts m. 167° (decomposition), [α]D ± 10.6° (H2O, c 10).

IT 105601-04-5P
RL: SPN (Synthetic preparation); PRP (Properties); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(Resolution of α-m-hydroxyphenylethylmethylamine and the preparation of d- and l-miotine (methylurethans of d- and l-α-m-hydroxyphenylethyldimethylamine))

RN 105601-04-5 CAPLUS
CN Phenol, 3-[1-(dimethylamino)ethyl]- (CA INDEX NAME)



IT 5441-61-2P, Phenol, m-(α-dimethylaminoethyl)-, -HCl
RL: PREP (Preparation)
(preparation of)
RN 5441-61-2 CAPLUS
CN Phenol, 3-[1-(dimethylamino)ethyl]-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

L8 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1929:29266 CAPLUS
DOCUMENT NUMBER: 23:29266
ORIGINAL REFERENCE NO.: 23:3451e-i,3452a-c
TITLE: Methylurethans of the isomeric α-hydroxyphenylethyldimethylamines and their Miotic activity
AUTHOR(S): Stedman, Edgar; Stedman, Ellen
SOURCE: Journal of the Chemical Society (1929) 609-17
CODEN: JCSOA9; ISSN: 0368-1769
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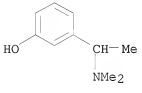
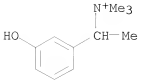
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 23:29266
AB The substances heretofore examined include 2 series of isomeric methylurethans, viz., the dimethylaminophenyl esters of methylcarbamic acid. HNMeCO2C6H4NMe2, and the methylurethans of the hydroxybenzyldimethylamines, NHMeCO2C6H4CH2NMe2. None of the compds. of these series contains an asym. C, and in view of the known difference in activity of the enantiomorphs of certain physiol. active substances, expts. have been carried out with the object of introducing such asymmetry into the latter of the above series of isomerides. For this purpose, the methylurethans of the isomeric α-hydroxyphenylethyldimethylamines have been prepared, this particular series being chosen because the introduction of an asyim. C is effected with the min. structural alterations necessary for this purpose. Unfortunately, these urethans have not yet been obtained in optically active forms. In the meantime, the results obtained with the dl-bases are here recorded. The 3 isomeric urethans were prepared by conversion of the methoxybenzaldehydes into the methoxyphenylmethylcarbinols via Grignard, followed by treatment with HBr; the corresponding bromides thereupon react with Me2NH to give the α-methoxyphenylcthyldimethylamines, which on demethylation by HBr yielded the phenols and finally the methylurethans, NHMeCO2C6H4CHMeNMe3, by interaction with MeNCO under appropriate conditions. The following compds. are described: m-methoxyphenylmethylcarbinol, b14.5 133°;

α-m-methoxy-methoxyphenylethydimethylamine. b17 118-9° (HCl salt. m. 105°: methiodide, C12H20ONI, pale cream, m. 142°); α-m-hydroxyphenylethyldimethylamine, m. 87-8° (HCl salt, C10H15ON.-HCl, m. 197-8°; methiodide, micro-crystalline, m. 160°); α-o-methoxyphenylethyldimethylamine, b12 105-7°, b13.5 103.5° (HCl salt, an oil; methiodide, C14H10ONI, m. 136-7°); α-O-hydroxyphenylethyldimethylamine, b14 112-4° (HCl salt, C10H17ON.HCl, m. 136-7°; α-p-methoxyphenylethyldimethylamine, b14 118° (HCl salt, C11H17ON.HCl, m. 213°; methodide, m. 128-30°); di[α-p-methoxyphenylethyl]dimethylammonium bromide, C20H26O2NBr.H2O, thick plates, m. 109°; α-p-hydroxyphenylethyldimethylamine, m. about 115° (HBr salt, m. 178°; HCl salt, C10H15ON.HCl, m. 183°). Methylurethan of α-m-hydroxyphenylethyldimethylamine, C12H14O2N2, m. 86° (HCl salt, m. 160° (effervescence); methiodide, C13H21O2N2I, m. 130° (effervescence)). Methylurethan of α-o-hydroxyphenylethyldimethylamine, m. 90° (HCl salt (I) extremely hygroscopic; methiodide, C13H21O2N2I, m. 148° (effervescence)). Methylurethan of α-p-hydroxyphenylethyldimethylamine, unknown in free state (HCl salt, C12H18O2N2.HCl, m. 203°; methiodide (II), m. 173° (effervescence)). The 3 urethans have been tested for miotic activity in the form both of their HCl salts and methiodides by instillation into cats' eyes, 1.5% solns. of these substances in physiol, salt solns. being employed. In case of (I) the free urethan was dissolved in the calculated amount of 0.153 N HCl and diluted to 1.5% with physiol. salt solution With the exception of (II), which had no action at this dilution, a contraction of the pupil resulted in each case, the extent of the miosis differing with the various substances employed. The estimated order of activity is: m-HCl > o-MeI > p-HCl, o-HCl, m-MeI > p-MeI. This order can of course only be regarded as provisional until the activities on other organs have been compared. It should, however, be noted that the observed activities of p-HCl, o-HCl, m-MeI were quite small in the dilns. used, the m-HCl and o-MeI being very much greater. The miotic activity of m-HCl was intense and persistent, probably approaching that of physostigmine.

IT 105601-04-5, Phenol, m-(α-dimethylaminoethyl)-
(and derivs.)
RN 105601-04-5 CAPLUS
CN Phenol, 3-[1-(dimethylamino)ethyl]- (CA INDEX NAME)




IT 860737-04-8P, Ammonium, (m-hydroxy-α-methylbenzyl)trimethyl-, iodide
RL: PREP (Preparation)
(preparation of)
RN 860737-04-8 CAPLUS
CN Benzenemethanaminium, 3-hydroxy-N,N,N,α-tetramethyl-, iodide (1:1) (CA INDEX NAME)


N+Me3
HO
CH—Me


I−